ASAS Centennial Paper: Developments and future outlook for preharvest food safety

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ASAS Centennial Paper: Developments and future outlook for preharvest food safety[1]

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ABSTRACT: The last century of food animal agriculture is a remarkable triumph of scientific research. Knowledge derived through research has resulted in the development and use of new technologies that have increased the efficiency of food production and created a huge animal production and food manufacturing industry capable of feeding the US population while also providing significant quantities of high-quality food for export to other countries. Although the US food supply is among the safest in the world, the US Center for Disease Prevention and Control estimates that 76 million people get sick, more than 300,000 are hospitalized, and 5,000 die each year from foodborne illness. Consequently, preventing foodborne illness and death remains a major public health concern. Challenges to providing a safe, abundant, and nutritious food supply are complex because all aspects of food production, from farm to fork, must be considered. Given the national and international demand and expectations for food safety as well as the formidable challenges of producing and maintaining a safe food supply, food safety research and educational programs have taken on a new urgency. Remarkable progress has been made during the last century. Wisdom from a century of animal agriculture research now includes the realization that on-farm pathogens are intricately associated with animal health and well-being, the production of high-quality food, and profitability. In this review, some of the developments that have occurred over the last few decades are summarized, including types, sources, and concentrations of disease-causing pathogens encountered in food-producing animal environments and their association with food safety; current and future methods to control or reduce foodborne pathogens on the farm; and present and future preharvest food safety research directions. Future scientific breakthroughs will no doubt have a profound impact on animal agriculture and the production of high-quality food, but we will also be faced with moral, ethical, and societal dilemmas that must be reconciled. A strong, science-based approach that addresses all the complex issues involved in continuing to improve food safety and public health is necessary to prevent foodborne illnesses. Not only must research be conducted to solve complex food safety issues, but results of that research must also be communicated effectively to producers and consumers.

Key words: *Campylobacter jejuni*, *Escherichia coli* O157:H7, foodborne pathogen control, *Listeria monocytogenes*, preharvest food safety, preharvest food safety research

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INTRODUCTION

Knowledge derived through research in the last century has resulted in the development and use of new technologies that have markedly increased the efficiency of food production and created a huge animal production and food manufacturing industry capable of feeding the US population while also providing significant quantities of high-quality food for export to other countries. Advances have brought exciting new technologies that can or will be used to solve complex problems confronting animal agriculture. These advances have had a fundamental impact and have revolutionized production agriculture systems. Increased animal growth, efficiency, and productivity; improved husbandry and management procedures; improved disease surveillance; enhanced disease resistance; and manipulation of food

[1]Proprietary or brand names are necessary to report factually on available data; however, the USDA neither guarantees nor warrants the standard of the product, and the use of the name by the USDA implies no approval of the product, or exclusion of others that may be suitable.

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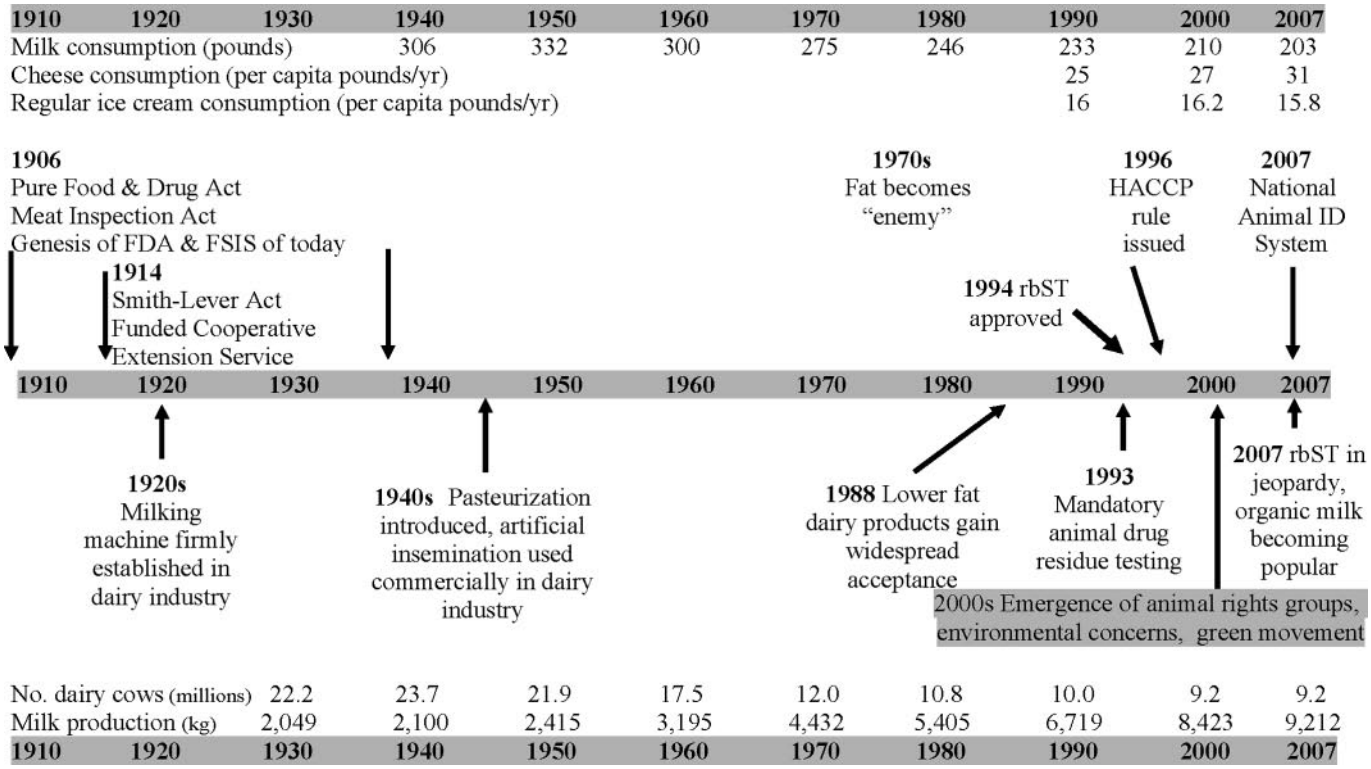

Figure 1. Advances in and challenges to the dairy industry during the existence of the American Society of Animal Science. Data from USDA-National Agricultural Statistics Service and USDA-Economic Research Service, Washington, DC. rbST = recombinant bovine ST.

quality and quantity are only a few areas that have affected food animal agriculture. For example, much of the progress in the dairy industry has been due to advances in biological technology. Scientific feeding of cows, mechanical milking, genetic selection and AI, and the discovery and implementation of mastitis control procedures are just a few technological advances that have had a huge impact on the dairy industry. The impact and magnitude of these advances are perhaps best appreciated when considering that total milk production in the United States is nearly 60% greater today than in 1950, with 58% fewer cows (Figure 1). Similar advances have had a profound impact on the beef industry, with feed efficiency nearly 50% greater today than in the 1950s (Figure 2). This demonstrates quite clearly that technological advances have had a profound impact on food animal agriculture.

Issues such as animal health, human health, the sustainability of animal agriculture, and the role of regulatory and public health agencies have dominated the agenda over the years (Ravenel et al., 1926; White, 1964; Lake, 1970; Roberts, 1970) and continue to be relevant today (Fennema, 1990; Bryan, 2001; Oliver et al., 2005). More recently, epidemiology, farm biosecurity, food safety, and environmental protection dominate an increased proportion of our research and policy focus. Despite this paradigm shift, the fundamental issues facing food animal agriculture remain the same (Beier and Pillai, 2005; Doyle and Erickson, 2006). The bottom line is, how do we enhance food production as well as animal health and ensure public health and sustainable agriculture with the least burden to taxpayers? To balance all this has been and continues to be a formidable challenge.

More than 200 known diseases are transmitted through food by a variety of agents, including fungi, viruses, parasites, and bacteria. The threats are numerous and varied, such as *Escherichia coli* O157:H7 in meat and apple juice; *Salmonella* in eggs and on meat, vegetables, and poultry; *Campylobacter* in poultry, swine, and cattle; *Vibrio* in shellfish; *Cyclospora* and the hepatitis A virus on fruit; *Cryptosporidium* in drinking water; the safety and consumer perceptions of genetically modified foods; the impact of farming practices on chemical uptake in food; the migration of agricultural chemicals through soil, air, and water; and the overall impact of farming practices on human health.

Foodborne illness is a major factor contributing to morbidity and mortality in the United States and worldwide. Advances in science and technology, food production, and processing have made the food supply in the United States one of the safest in the world. However, in spite of this, every year people die and countless others suffer because of breaches in food safety. Consequently, the economic and public health burden of foodborne disease remains substantial [Economic Research Service (**ERS**), 2000). Estimates of food-related illness and deaths in the United States indicate that foodborne diseases cause approximately 76 million illnesses, 325,000 hospitalizations, and 5,000 deaths each year (Mead et al., 1999). The demographic picture of the United States is also changing rapidly,

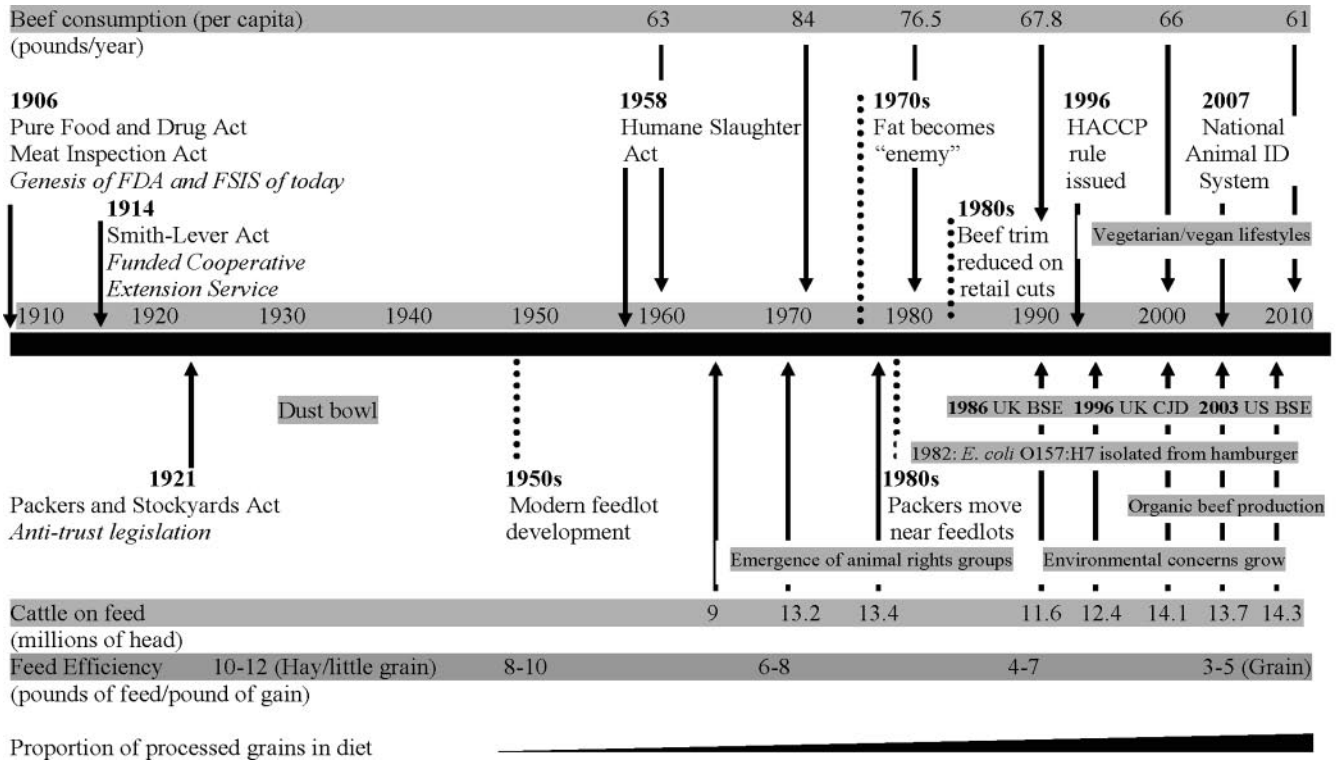

Figure 2. Challenges faced by the beef industry during the existence of the American Society of Animal Science. Data from USDA-National Agricultural Statistics Service, Washington, DC.

with an increasing number of elderly people and immunocompromised individuals who are more susceptible to foodborne pathogens. A major challenge in food safety today is the complexity of the problem, because many zoonotic and nonzoonotic sources of microbial pathogens could breach the food safety barrier. Food safety begins with the soil, plant, or animal, and continues within the plant or animal through various stages of production and processing. Maintaining food safety is further exacerbated by the myriad methods of food production, processing, storage, distribution, and service; the variety of foods available and demanded; and the number of people involved with food preparation. Thus, it is evident that reducing the bacterial pathogen contamination of our food supply could save both lives and billions of dollars in costs annually.

The multibillion-dollar costs, together with the increasing frequency of foodborne disease outbreaks and the need for a modern system of food inspection, prompted a massive reform for pathogen reduction that resulted in implementation of the Hazard Analysis Critical Control Points System, more commonly referred to as **HACCP**. Consequently, there has been a surge of research activity into pathogen reduction strategies that were mainly inspired by the HACCP initiative. The nature of these systems affects not only food-processing plants, but also the food production unit, because this system is based on the evaluation of raw product received from the producer. In January of 2000, all food-processing plants were required to have an HACCP system in place that included the ability to trace foodborne pathogens back to the production unit. Thus, the food production unit needs a system(s) to detect the origin of the contamination as well as effective measures to reduce microbial contamination.

Food can become contaminated by a variety of factors (zoonotic or nonzoonotic, direct or indirect; Figure 3). It is apparent that many factors are beyond the farm environment and farm operations and involve other aspects of food delivery, logistics, training, and education. Nevertheless, farm-associated pathogenic bacteria are directly or indirectly associated as risk factors in the entire commercial food chain. For example, pathogens carried on the hides or skin of animals or their raw products introduce pathogens into the food production environment. This may lead to direct contamination caused by faulty methods of food preparation or inadequate processing, or by indirect contamination through a buildup in the environment as biofilms. Animal activity on the farm, manure management, and effluent discharge influence bacterial populations in farm soil as well as associated pathogenic flora. Salad greens often harbor animal pathogens, and inadequate sanitation or treatment washes may lead to the presence of pathogens in the finished produce. Consumers rightfully deserve and expect a safe product each time, all the time. From a public health point of view, a reduction in foodborne and associated illnesses is paramount. To achieve this goal, animal farm operations need to share in their responsibility of producing a safe, healthy, and nutritious product. To address this goal in a practical and economical framework is a significant challenge for

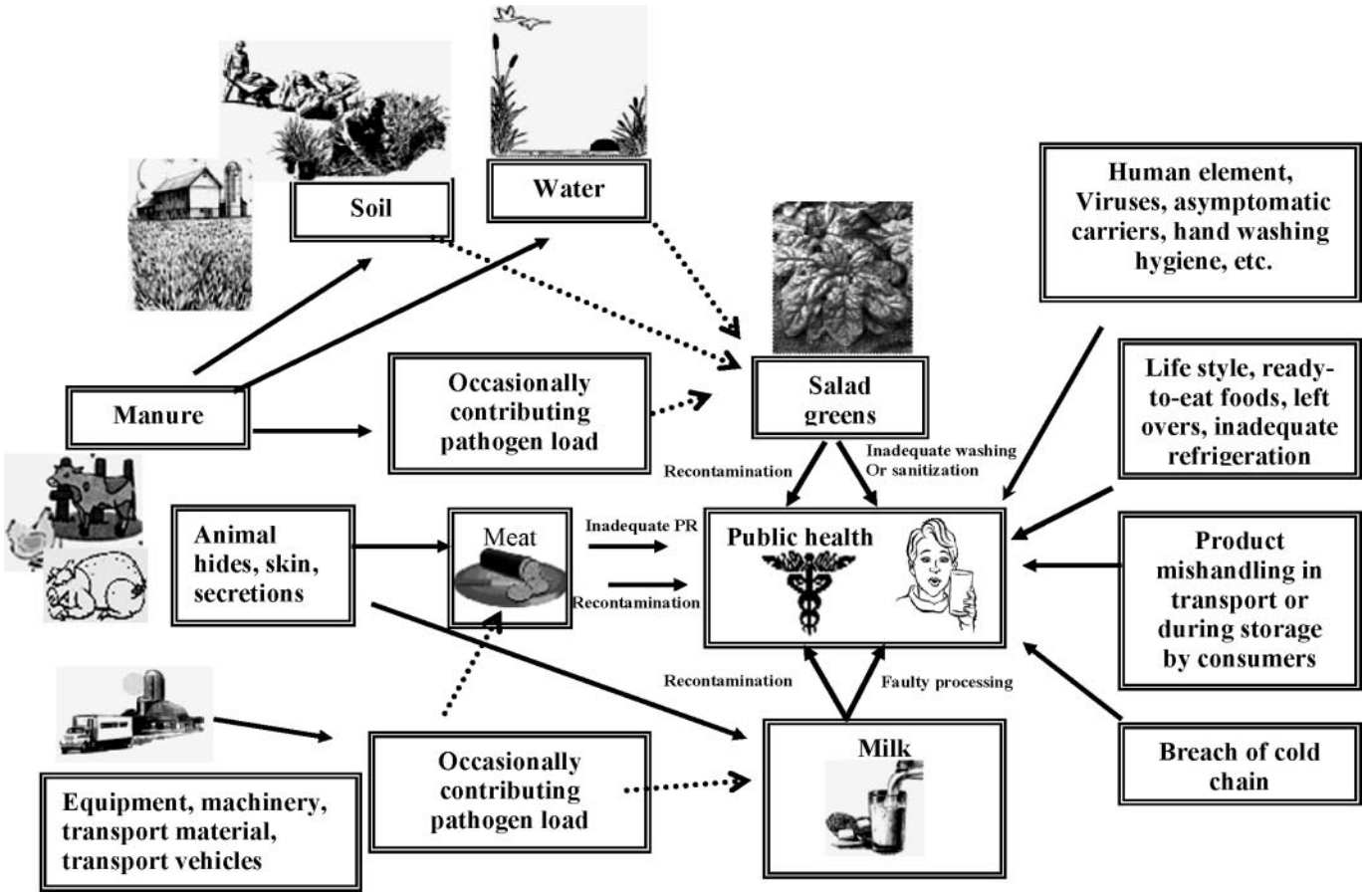

Figure 3. Impact of farm-associated direct and indirect factors and other nonfarm factors on food safety.

all stakeholders, including government, academia, the food and farm industry, consumers, and other advocacy groups.

New technologies to reduce bacterial contamination based on prebiotics or probiotics for competitive gut exclusion seem promising. Animal certification programs, herd testing and improvement initiatives, diagnose-detect and cull strategies, mastitis control measures and quality milk production, and improved treatment or therapeutic strategies are a few of the farm control measures affecting animal health and food safety. New tools for pathogen detection and pathogen modeling hold considerable promise for influencing research and measurable outcomes in food safety (Wiedmann, 2003). If the progress encountered in the past century is any indication of the future, we should anticipate that marked progress will be made. However, in all likelihood, interventions based on biotechnology or nanotechnology will be developed, and ideally, these new interventions will be debated in a constructive and rational manner so that science-based solutions to complex issues can emerge. In this review, developments that have occurred over the last few decades are summarized, including types, sources, and concentrations of disease-causing pathogens encountered in food-producing animal environments and their association with food safety; current and future methods to control or reduce foodborne pathogens on the farm; and present and future preharvest food safety research directions.

FOODBORNE PATHOGENS OF INTEREST

Many foodborne pathogens can have habitats in food-producing animals (e.g., skin and gastrointestinal tracts) and in the farm environment. These pathogens can enter meat and milk products during slaughter or at milking, or can contaminate raw vegetables when soil is fertilized with improperly composted (or uncomposted) animal manure (McEwen and Fedorka-Cray, 2002). There is evidence to support the concept that the significant increase in the incidence of foodborne illness is related to changes in animal husbandry practices and to the handling and processing of foods of animal origin (Elder et al., 2000; Hynes and Wachsmuth, 2000; Committee on the Review of the Use of Scientific Criteria and Performance Standards for Safe Food, National Research Council, 2003; Beier and Pillai, 2005). Microorganisms are found throughout the food-producing animal environment, and new bacteria are being discovered continuously (Rappe et al., 1998; Stingl and Giovannoni, 2005). Specific groups of disease-causing microorganisms are consistently associated with the food-producing animal environment. Years of epide-

miologic and zoonotic research have provided valuable information about significant farm pathogens that need to be monitored closely.

From the standpoint of preharvest food safety in general and human health in particular, *Salmonella* spp., *E. coli*, *Campylobacter jejuni*, and *Listeria monocytogenes* are important foodborne pathogens affecting public health (Bean and Griffin, 1990; Mead et al., 1999; Bryan, 2001). According to the Centers for Disease Control and Prevention, these pathogens are the leading causes of foodborne morbidity and mortality. Dairy and beef cattle can harbor and shed *E. coli* O157:H7, yet animals can remain asymptomatic. C*ampylobacter jejuni*, *L. monocytogenes*, and *Salmonella* spp. are carried by cattle, poultry, and swine and are found in their associated farm environments (Figure 3). Epidemiological data suggest that other pathogens, including *Staphylococcus aureus*, *Clostridium perfringens*, and *Bacillus cereus* are important pathogens that have origins on farms. The *Streptococcus suis* encountered in swine production is now recognized as a human pathogen. Viruses such as norovirus and hepatitis E, and parasites such as *Cryptosporidium purvum* and *Toxoplasma gondii* that are encountered in the farm environment are considered emerging pathogens because of their negative association with human health (Tauxe, 2002; Koopmans and Duizer, 2004).

The major pathogenic bacteria of animal origin transmitted through food in the United States include *Salmonella*, *E. coli*, *C. jejuni*, and *L. monocytogenes* (Wesley, 2006). These pathogens are found in animal feces (Murinda et al., 2004; Hutchison et al., 2005); therefore, contamination of carcasses and food products by animal feces is likely to be a principal mode by which foodborne pathogens reach the consumer. Cattle, sheep, swine, chickens, and turkeys are principal reservoirs, but wild birds and various mammals that are common in farm environments can also be a source of these pathogens (D'Aoust et al., 2008; Meng et al., 2008; Nachamkin, 2008; Swaminathan et al., 2008). The contamination cycle in food-producing animals is through ingestion of contaminated feeds and water that can be contaminated by feces. The use of nontreated manure as fertilizer, the spread of slurry, and the use of recycled wastewater disseminate these pathogens even more. Stresses on animals caused by poor management and the types and quantities of animal feeds increase susceptibility to infection and shedding of foodborne pathogens (Cray et al., 1998). All these environmental and management factors should be considered when attempting to identify farm practices and critical control points on the farm where contamination occurs, and then appropriate interventions can be implemented.

Salmonella spp. have been linked with illness among many animal species and humans, and are one of the most commonly reported causes of human foodborne disease (Bean and Griffin, 1990). *Salmonella* live in the intestinal tract of various animal species and therefore represent a major reservoir for human foodborne disease. Studies have shown that *Salmonella* infection may be present on farms in the absence of clinical disease. In beef cattle, *Salmonella* was detected in 38 of 100 feedlots and in 21 of 187 beef cow-calf operations (Fedorka-Cray et al., 1998; Dargatz et al., 2000). On swine farms, *Salmonella* was detected on 58 of 152 farms, with a greater prevalence observed in states in the Southeast (65.5%) compared with states in the Midwest (29.9%; Bush et al., 1999). Poultry is considered an important source of *Salmonella*. In a nationwide broiler chicken and raw ground chicken microbiological baseline data collection by USDA-Food Safety and Inspection Service, *Salmonella* was detected in 20% of broiler carcasses and 45% of ground chicken meat (Rabsch et al., 2003). In addition, healthy animals can become carriers and shed *Salmonella* for long periods. Humans become infected primarily through fecal contamination of food products or water; however, direct contact with infected animals is another source of contamination, especially for farm families. Although a great percentage of human salmonellosis occurs through consumption of raw milk or dairy products manufactured with raw milk, human illnesses are frequently linked with consumption of poultry and pork products (Vugia et al., 2007). Many of the >2,500 *Salmonella enterica* serotypes are isolated frequently from clinically infected animals. *Salmonella enterica* serovars Typhimurium, Enteritidis, Javiana, Hadar, Kentucky, and Anatum are among these serotypes, and *Salmonella* Typhimurium DT 104 is of particular concern to public health agencies because of its multiple antibiotic resistance genes (Besser et al., 2000).

Because fecal shedding of *Salmonella* is one of the principal modes of on-farm contamination (Murinda et al., 2002a), the question of how fecal shedding can be reduced is very relevant to human health. Research has demonstrated that reduction of *Salmonella* fecal shedding in poultry and swine production units is possible through the modification of management practices. A common approach used in the control of infectious disease is identifying infected and carrier animals and culling them from the herd. However, widespread distribution of *Salmonella* in the environment hampers the success of identification-and-culling programs. Therefore, it seems more appropriate to use identification and removal of infectious sources and the adoption of quality assurance programs that ensure use of this process, such as HACCP-based programs. This approach also has limitations, because *Salmonella* appear to be established in several environments. For instance, *Salmonella* have been shown to be common in outflows from human sewage treatment plants, with the possibility of surface water contamination and contamination of animals downstream. In addition, animal feeds may be contaminated off site with *Salmonella* because the use of untreated manure for fertilization of grain or forage-producing farmland is common (McChesney et al., 1995). Wild birds and rodents also have been described as sources of *Salmonella* contamination (War-

nick et al., 1996; Murinda et al., 2004). Collectively, all these factors complicate the development of control strategies, because a prevention program should include all farm environment inputs. However, several control points that could be important for on-farm reduction of *Salmonella* include the presence of carrier animals, the exposure of neonates to feces from sick animals, environmental hygiene, the use of recycled water, contaminated feeds, the use of contaminated water to irrigate forage crops, the spreading of nontreated manure, and infected birds and rodents.

Several strains of *E. coli* cause a variety of diseases in humans and animals. *Escherichia coli* O157:H7 is a type associated with a particularly severe form of human disease. Enterohemorrhagic *E. coli* infection can lead to hemorrhagic colitis, hemolytic uremic syndrome, and thrombotic thromocytopenic purpura. This type of *E. coli* was first identified as a human pathogen in 1982 and as the etiology of human diseases that range from hemorrhagic colitis to life-threatening hemolytic uremic syndrome. Healthy cattle sporadically harbor *E. coli* O157:H7 in their gastrointestinal tracts, shedding this pathogen in their feces. The majority of human outbreaks caused by *E. coli* O157:H7 were linked to the consumption of contaminated ground meat and raw milk (Dorn, 1993; Boyce et al., 1995). Still, in several outbreaks a variety of nonruminant foods were identified as the source of contamination, although in many of these, the source of *E. coli* O157:H7 was traced to ruminant manure. For instance, the outbreak that occurred in 1991 in Massachusetts and the multistate outbreak that occurred in 1996 were found to be directly linked to the use of contaminated manure as fertilizer (Besser et al., 1993; Centers for Disease Control and Prevention, 1996). In another outbreak associated with contaminated vegetables, it was found that vegetables were grown in soil layered with manure contaminated with *E. coli* O157:H7 (Tarr, 1995). Fecal contamination of meat at slaughter plants and cross-contamination of other food products at retail shops were indicated as another possible source of contaminated foods. In addition, direct contact with ruminant feces has been associated with *E. coli* O157:H7 human infections on farms (Banatvala et al., 1996). Thus, cattle are currently considered a reservoir for *E. coli* O157:H7, and manure is an important vehicle for spreading contamination. *Escherichia coli* O157:H7 is also detected in other hosts, such as sheep, goats, horses, dogs, reindeer, deer, birds, and rabbits (Hancock et al., 1998; Pritchard et al., 2001). However, the association of domestic and wild animals in the epidemiology of *E. coli* O157:H7 in cattle remains unknown.

The prevalence of *E. coli* O157:H7 in cattle has been reported to be 0.3 to 6.1%, and the average time that the feces of an animal remained culture positive was 30 d (Wells et al., 1991; USDA-Animal and Plant Health Inspection Service, 1997). However, some animals remained intermittently culture positive for more than 1 yr (Zhao et al., 1995). The influence of the diet (grains vs. forage) on the shedding of Shiga toxin-producing *E. coli* in feces suggests that an amplification stage also occurs in the gastrointestinal tract of ruminants. The terminal rectum of the gastrointestinal tract is an important site where this pathogen has shown specific tropism (Naylor et al., 2003). *Escherichia coli* O157:H7 was detected in the terminal rectum, regardless of whether animals were experimentally or naturally infected. The pathogen was detected in feces up to 4 wk after experimental inoculation or up to 22 d in those that cohabited with infected animals. These findings led authors to propose the existence of "supershedders," and colonization of the terminal rectum was a precondition for this status (Naylor et al., 2003). Thus, it is very likely that feces from infected cattle serve as a primary source for *E. coli* O157:H7 contamination of food products. In fact, there are reports indicating that contamination of nonruminant feed sources is most often from ruminant manure (Tarr, 1995). Effluents from dairy farm operations include raw manure and slurry (a mixture of manure, urine, feed, and water). These effluents are often used as fertilizer for land used for growing corn for silage, grazing, or cultivation. Unless appropriately treated, manure is a potential biohazard capable of transmitting infective agents, including *E. coli* O157:H7, to humans and animals (Murinda et al., 2002b). The current opinion is that because of the link to bovine products, cattle are thought to be a principal reservoir of *E. coli* O157:H7.

Several investigations aimed at the identification of possible intervention strategies to control the prevalence of *E. coli* O157:H7 on farms have linked production practices (critical points) with persistence of this foodborne pathogen in cattle and the generation of reservoirs in the farm environment (Garber et al., 1995; Zhao et al., 1995; Hancock et al., 1997; Shere et al., 1998; Elder et al., 2000; Arthur et al., 2007). Among these, diet (Cray et al., 1998; Diez-Gonzalez et al., 1998), age of cattle (Cray and Moon, 1995; Garber et al., 1995), management of manure and fecal slurry, contaminated animal drinking water (Faith et al., 1996; Shere et al., 1998; Murinda et al., 2002b; Murinda et al., 2004), and management of pre- and postweaned calves (Garber et al., 1995; Faith et al., 1996; Shere et al., 1998) have been identified as risk factors for the infection and shedding of *E. coli* O157:H7 by cattle.

Especially important is the use of manure as fertilizer or contaminated water to irrigate field crops. Contaminated manure and irrigation water were probable vehicles for the pathogen in many human disease outbreaks. Supporting data were obtained from a study in which the occurrence and persistence of *E. coli* O157:H7 was determined on lettuce and parsley grown in soil fertilized with contaminated poultry or bovine manure composts or treated with contaminated irrigation water. Results from this study indicated that *E. coli* O157:H7 could persist for 154 to 217 d in soils fertilized with contaminated composts. After seedlings were planted, *E. coli* O157:H7 could be detected on lettuce and pars-

ley for up to 77 and 177 d, respectively. In addition, *E. coli* O157:H7 persisted in soil for more than 5 mo after application of contaminated compost or irrigation water, regardless of the source or crop type (Islam et al., 2004).

Campylobacter is the most frequently identified cause of acute infectious diarrhea in developed countries and is the most commonly isolated bacterial intestinal human pathogen in the United States. It has been estimated that between 2 and 4 million cases of campylobacteriosis occur each year, and *Campylobacter* is associated with 120 to 360 deaths. *Campylobacter jejuni* and *Campylobacter coli* are commonly foodborne and are the infectious agents most frequently described in association with Guillain-Barré syndrome. *Campylobacter* foodborne disease is characterized by sporadic cases of chronic gastritis, enterocolitis, and septicemia. Humans become infected by ingesting contaminated foods, untreated water, or contaminated nonpasteurized or improperly pasteurized milk (Fahey et al., 1995). Several zoonotic sources have been identified, and *C. jejuni* has been isolated from cattle, swine, poultry, dogs, cats, birds, ferrets, hamsters, wild birds, mule deer, and houseflies (Altekruse, 1994). The most common foodborne source of *Campylobacter* infection in humans remains poultry meat products (Vugia et al., 2007). The prevalence of *Campylobacter* in the United States is 32 to 53% in poultry, 45% in cattle, 6% in beef, and 27% in swine operations (Miller and Mandrell, 2005). Physiological characteristics of *Campylobacter* suggest that these organisms have evolved to optimally colonize the avian gut (Newell and Davison, 2003). The number of *Campylobacter* in feces can be as great as 10^{10} cfu/g (Cawthraw et al., 1996). Surveys of swine farms and abattoirs demonstrated a great prevalence of *Campylobacter* (70 to 89%) in intestinal or fecal samples (Young et al., 2000). *Campylobacter jejuni* is excreted in feces and animal secretions, and animals are infected through ingestion of water and feeds contaminated with manure. Enumeration studies have shown that a critical amplification stage in the *Campylobacter* cell cycle occurs in the intestines of asymptomatic animals. Once bacteria are excreted into the environment, they must use survival strategies until ingested by a susceptible host. Thus, the intestinal tract and feces of susceptible animals (carriers) are considered the major reservoir of this foodborne pathogen. In addition to the many outbreaks and isolates linked to poultry products (Jacobs-Reitsma, 1997; Atterbury et al., 2003b), several have been linked to pork and beef (Bolton et al., 1985; Zhao et al., 2001). Outbreaks linking *C. jejuni* with consumption of unpasteurized, contaminated milk have also been reported (Fahey et al., 1995; Djuretic et al., 1997; Centers for Disease Control and Prevention, 2001; Oliver et al., 2005). Direct excretion of *C. jejuni* in milk by clinically healthy cows was described and implicated in the etiology of human enteritis after the consumption of contaminated milk (Orr et al., 1995). A few reports on dairy farm management practices related to *C. jejuni* contamination of the environment and the role of these practices in the contamination of drinking water sources have been published (Stanley et al., 1998; Wesley et al., 2000; Murinda et al., 2004). Application of manure with broadcast spreaders; feeding of whole cottonseed, cottonseed hulls, or alfalfa; accessibility of feed to birds; and contamination of ground water with farm effluents contaminated by *C. jejuni* were identified as possible risk factors for *C. jejuni* infection. As with other foodborne pathogens, animal manure is a principal reservoir, and farm practices using manure as fertilizer or spreading manure on the ground of the farm are considered a significant risk factor for the occurrence of foodborne disease. In addition, an increasing proportion of human infections caused by *C. jejuni* are resistant to antimicrobial therapy (Altekruse et al., 1999).

Listeria monocytogenes causes serious foodborne illness (listeriosis) in humans at risk, primarily pregnant women and their fetuses, the elderly, and the immunocompromised. In addition, the resistance of the pathogen to antimicrobials has emerged as a public health concern. The World Health Organization informal working group on foodborne listeriosis indicated that foodborne listeriosis is transmitted predominantly by nonzoonotic means. Although the natural habitat of the organism appears to be the soil and vegetation, listeriosis cannot be categorically stated to be a soilborne disease. *Listeria monocytogenes* should be considered an environmental contaminant whose primary means of transmission to humans is through food, which can become contaminated during production and processing. However, the ultimate sources of such contamination and the relative contributions of food-producing animals remain unknown. Ready-to-eat (**RTE**) foods that are refrigerated before consumption and do not receive substantial treatment, such as soft cheese, RTE meats, and RTE seafoods, have been implicated in outbreaks of listeriosis (Kathariou, 2002). The cumulative 10-yr prevalence rate of *L. monocytogenes* based on USDA-Food Safety and Inspection Service microbiological testing of RTE meats and poultry products at approximately 1,800 federally inspected plants was as follows: uncured poultry products, 2.1%; cooked beef, roast beef, and cooked corned beef, 3.1%; jerky, 0.5%; large-diameter cooked sausage, 1.3%; small-diameter cooked sausage, 3.6%; salads, spreads, and pâtés, 3.0%; and sliced ham and luncheon meat, 5.2% (Levine et al., 2001). The species is partitioned into 2 major genomic divisions (lineages), and most clinical cases involve just 3 serotypes (1/2a, 1/2b, 4b; reviewed in Kathariou, 2002). This pathogen has been isolated from mammals, including sheep, cattle, swine, poultry, and dogs, as well as from birds, fish, crustaceans, and insects. The presence of *L. monocytogenes* on carcasses is usually attributed to contamination by fecal matter during slaughter. A large percentage (11 to 52%) of animals are reported to be healthy but silent carriers, whereas

healthy human intestinal carriers occur at a rate of 1 to 5% (Martin, 2003; Swaminathan et al., 2008). As many as 45% of pigs harbor *L. monocytogenes* in the tonsils, and 24% of cattle have contaminated internal retropharyngeal nodes (Skovgaard and Norrung, 1989; Buncić, 1991). In addition, *Listeria* spp. are widespread in nature and live naturally in plants and soil environments. *Listeria* can grow in a wide range of temperatures and pH. This adaptability enables *Listeria* to grow in refrigerated raw milk and in low-quality silos with a pH >4.5. At greater bacterial concentrations, *L. monocytogenes* can survive minimum high-temperature, short-time pasteurization (Bunning et al., 1988). *Listeria monocytogenes* can cause mastitis in cows and it can be shed in milk from all quarters of carrier asymptomatic cows. Similar to *E. coli* and *Salmonella*, human contamination occurs through consumption of raw milk or products manufactured with raw milk. In dairy and beef units, infection of animals occurs through ingestion of contaminated feed, especially low-quality and spoiled silage (Fenlon, 1985). In cattle, *L. monocytogenes* can cause neurological disease, abortion, or no symptoms of disease. Healthy but infected animals shed *Listeria* in feces, and fecal contamination of pastures or vegetables was also incriminated as a source of contamination for humans and ruminants. Therefore, farm practices, such as spreading of untreated manure, are regarded as risk factors for foodborne disease (Murinda et al., 2004).

What Do These Foodborne Pathogens Have in Common, and How Can They Be Controlled on Farms?

Several epidemiological characteristics are common to *Salmonella*, *E. coli* O157:H7, *C. jejuni*, and *L. monocytogenes*. Among these are the following:

- Foodborne pathogens are shed in feces and gastrointestinal secretions or excretions of healthy animals. Shedding is sporadic and is caused by reinfection from sources in the environment.
- Cattle, swine, and poultry are believed to be the primary reservoirs, but birds and various mammals that are common in farm environments were also identified as reservoirs.
- The contamination cycle is as follows: infection occurs initially by ingestion of contaminated feeds and water, followed by shedding of food pathogens in feces that, in turn, contaminate feeds and animal drinking water, causing new infections and reinfection of convalescent animals.
- Stress caused by poor management and by the types and quantities of animal feedstuffs increases their susceptibility to infection and the shedding of foodborne pathogens.
- Feeds and water contaminated with feces and secretions or excretions from animals are the vehicles for additional contamination in the environment, including other mammals, birds, and insects. The use of nontreated manure as fertilizer and the spread of slurry and recycled wastewater further disseminate contamination.

Information published thus far supports the model in which the presence of pathogens depends on ingestion of contaminated feed, followed by amplification in animal hosts and fecal dissemination in the farm environment (Figure 3). Colonization of the gastrointestinal tract and amplification of *E. coli* O157:H7, *Salmonella*, *C. jejuni*, and *L. monocytogenes* appear to be required stages in the cell cycles. Shedding of foodborne pathogens in feces and distribution in the environment where food-producing animals live lead to animal reinfection and persistence of the pathogen on the farm. This, coupled with infection of other mammals, birds, and insects that live on the farm, demonstrates that production units are major reservoirs for foodborne pathogens. The final outcome of this cycle is a constantly maintained reservoir of foodborne pathogens that can reach the human population by direct contact, ingestion of raw contaminated food, or contamination during the processing of milk. Isolation of bacterial pathogens with similar biotypes from farms and from outbreaks of human disease substantiates this hypothesis. Management of manure, which includes feces, urine, saliva, and other animal secretions or excretions, is central for the control of contamination in food-producing animals. By breaking the infection-reinfection cycle, it is possible to reduce foodborne pathogen shedding and therefore the spread of foodborne pathogens among food-producing animals and in the farm environment. Designing on-farm foodborne control programs based on the control of common points of transmission and the spread of foodborne pathogens should reduce the introduction of foodborne pathogens into processing plants. However, the lack of knowledge on critical control points where infection-reinfection and contamination occur hampers the development of on-farm foodborne control programs.

It is apparent that despite the complexity and diversity of the microbial community, major human pathogens with their origin in farm operations are now known. From a management point of view, it is practicable to focus on selected groups of pathogens. However, many of the pathogens are asymptomatic for the animal harboring or shedding them. Previous experience in pathogen reduction strategies, pathogen eradication strategies, or both amply testifies that postharvest packing or processing in itself is not adequate to reduce the risk of food safety consistently. Many experts now believe that pathogen reduction and HACCP strategies have resulted in noticeable changes in food safety risk reduction. It is imperative that even if human pathogens cannot be completely eliminated preharvest, their intended reduction is a logical end point that could reduce morbidity and mortality.

FOOD PATHOGEN INTERVENTION AND REDUCTION STRATEGIES

In addition to direct infection via food, the disconnect between consumers and their food supply is reflected in a growing number of direct-contact illnesses in humans contracted in farmyards, open farms, petting zoos, and zoological parks (Chapman et al., 2000; Keen et al., 2007). Recent years have seen an increase in human foodborne illnesses linked to water contaminated by runoff from farms (Public Health Agency of Canada, 2000; Jay et al., 2007). The spread of foodborne pathogens via runoff has been assessed only recently to understand the movement of pathogens from farms during rainfall events (Berry et al., 2007; Ferguson et al., 2007). Further concerns have been raised about the spread of pathogens to humans through crops (e.g., spinach or lettuce) irrigated with water from animal production facilities (Natvig et al., 2002; Gerba and Smith, 2005). The 2006 *E. coli* O157:H7 outbreaks from spinach and lettuce (Jay et al., 2007) highlight the ability of foodborne pathogens from food animals to be widely disseminated through the food chain, further emphasizing the need to reduce foodborne pathogenic bacteria in the live animal before they contact human consumers (Hynes and Wachsmuth, 2000; Loneragan and Brashears, 2005; Sargeant et al., 2007). With the growing industrialization of the production and transport of food, human illnesses from indirect contact have become increasingly noted, from *Salmonella* in peanut butter and tomatoes to *Campylobacter* in raspberries.

Current Strategies to Reduce Foodborne Pathogens in Food Animals

Some of the most promising improvements aimed at enhancing food safety have focused on the development of interventions that work at the live-animal level. Live-animal, or on-farm, intervention strategies can be loosely grouped into 2 categories: procommensal strategies or directly antipathogen strategies. Procommensal strategies use a native (or introduced) microbial ecosystem against pathogens by capitalizing on competition for nutrients and environmental niches. Directly antipathogenic strategies, on the other hand, specifically kill (or inhibit) pathogens via a variety of mechanisms.

Current Procommensal Strategies

A procommensal strategy is defined as the establishment of a nonpathogenic microbial intestinal population that reduces, excludes, or kills pathogenic bacteria, including foodborne pathogens. Simply put, procommensal strategies promote the growth of groups of bacteria that are competitive with, or even antagonistic to, the pathogens of interest. The goal of procommensal methods in food animals is simply to fill all ecological niches within the gut, preventing opportunistic pathogens from colonizing or remaining within the gut.

Procommensal strategies used in food animals include probiotics, which are microbial cultures that are fed to animals to maintain a constant flow of commensal organisms through the gut environment; competitive exclusion (**CE**), defined as the establishment of a microbial population in a naive food animal gut; and prebiotics. Unfortunately, all too often the benefits of procommensal strategies have been squandered by using cheaper antibiotics, which can alter the gut microbial ecology (Steer et al., 2000). However, because of increasing fears concerning the dissemination of antimicrobial resistance, it is expected that in the future, prophylactic antibiotic use in food animals will become more closely regulated and economically expensive, causing procommensal strategies to become more feasible and more widely accepted across the food animal production industry.

Probiotics

Probiotics are a broad category of products included in animal rations that are defined as a "live microbial feed supplement which beneficially affects the host animal by improving intestinal microbial balance" (Fuller, 1989). An alternative definition of a probiotic is "preparation of or a product containing viable, defined microorganisms in sufficient numbers, which alter the micro-flora (by implantation or colonization) in a compartment of the host and that exert beneficial health effects in the host" (Schrezenmeir and De Vrese, 2001). Today, hundreds of probiotics are marketed for use in humans and food animals to provide a broad spectrum of benefits, and these are usually 1) live cultures of yeast or bacteria, 2) heat-treated (or otherwise inactivated) cultures of yeast or bacteria, or 3) fermentation end products from incubations of yeast or bacteria.

Foodborne pathogens have been reported to be affected by some probiotic products (Ohya et al., 2000; Brashears and Galyean, 2002; Tkalcic et al., 2003). Swine are stricken by postweaning *E. coli* diarrhea, which causes significant morbidity and mortality (Amezcua et al., 2002). A culture of *Lactobacillus casei* significantly reduced *E. coli* diarrhea symptoms in gnotobiotic pigs (Bomba et al., 1999; Kyriakis et al., 2001). Other types of probiotic cultures have subsequently been used to reduce postweaning *E. coli* diarrhea in swine as well (Kyriakis et al., 2001). The use of probiotics to control foodborne pathogens specifically has been limited because there has been no economic incentive for producers to limit pathogen populations. Outbreaks and lawsuits have since provided adequate incentives; however, probiotics still must demonstrate production enhancement to be economically successful, and few of these commercially successful probiotics have been demonstrated to reduce foodborne pathogens effectively.

The cattle industry has used probiotics widely for many years to increase growth rate, milk production, and production efficiency (Tournut, 1989; Dawson et al., 1990; Yoon and Stern, 1996). In research comparing several commercially available probiotics, Keen and Elder (2000) found that these probiotics provided neither a benefit nor a detriment to *E. coli* O157:H7 shedding in cattle. A commercial *Saccharomyces cerevisiae* direct-fed microbial (**DFM**) culture reduced *E. coli* O157:H7 populations in batch culture, but not in a continuous flow culture system that simulated the bovine gut (Bach et al., 2003). A probiotic that contained *Streptococcus faecium* or a mixture of *S. faecium*, *Lactobacillus acidophilus*, *L. casei*, *Lactobacillus fermentum*, and *Lactobacillus plantarum* significantly reduced fecal shedding of *E. coli* O157:H7 in sheep from 2 to 4 $\log_{10}$ cfu/g of feces, but a *L. acidophilus* monoculture was ineffective in this study (Lema et al., 2001). Other researchers demonstrated that a DFM *L. acidophilus* culture isolated from cattle ruminal fluid reduced *E. coli* O157:H7 shedding by more than 50% when provided to feedlot cattle (Brashears and Galyean, 2002; Brashears et al., 2003a,b). In a further refinement of this DFM, when *L. acidophilus* cultures were combined with *Propionibacterium freudenreichii*, the prevalence of *E. coli* O157:H7 in feces and on hides was reduced by approximately 50% and 3-fold, respectively (Elam et al., 2003; Younts-Dahl et al., 2004; Stephens et al., 2007). Research has shown this DFM to improve the growth efficiency of cattle such that it economically balances the cost of its inclusion in cattle rations thus making a food safety enhancement economically viable.

CE

In neonatal animals, the digestive tract is initially sterile but is quickly colonized by gastrointestinal microflora from the environment or the dam (Jayne-Williams and Fuller, 1971; Fuller, 1989). Once a stable intestinal population is established, the gut is more resistant to pathogen colonization (Fuller, 1989). This effect of a microbial population has been described as "bacterial antagonism" (Freter et al., 1983). Competitive exclusion is a technique that involves the presentation of a nonpathogenic mixed bacterial culture to the intestinal tract of neonatal food-producing animals to colonize the gastrointestinal tract and provide pathogen exclusion (Fuller, 1989; Nurmi et al., 1992; Steer et al., 2000). Depending on the maturity of the gut and food animal species, the goal of CE can be the exclusion of pathogens from the naive gut of a neonatal animal or displacement of an established pathogenic population (Nurmi et al., 1992). As is typical of Darwinian selection, there are several proposed modes of action for CE in eliminating pathogenic bacteria, but the most likely appear to be 1) direct and indirect competition for limiting nutrients, 2) competition for physical attachment sites along the epithelial wall, and 3) the production of antimicrobial compounds, including colicins, bacteriocins, antibiotics, and VFA.

Competitive exclusion is effective across several animal species, but most CE research has focused on controlling *Salmonella* in newly hatched chicks. *Salmonella* colonization in chickens was reduced by administration of a CE preparation of bacteria derived from the gut of healthy adult chickens (Nurmi and Rantala, 1973). Other CE cultures similarly isolated have provided some protection against pathogen colonization in newly hatched poultry (Lloyd et al., 1977; Weinack et al., 1982; Nisbet et al., 1993; Stavric and D'Aoust, 1993). In the United States, a mixed commercial CE product composed of several defined species of bacteria (Preempt, MS BioScience, Dundee, IL) has been used to reduce the *Salmonella* colonization of chicks (Nisbet et al., 1993, 1996).

In swine, a *S. faecium* CE culture reduced intestinal colonization by diarrheagenic enterotoxigenic *E. coli* (Underdahl et al., 1982; Ushe and Nagy, 1985). Other researchers found that adding a mixed CE culture reduced *Salmonella* populations in newly weaned pigs (Fedorka-Cray et al., 1999). A cecally derived swine CE culture reduced the incidence of *Salmonella cholerasuis* (Anderson et al., 1999) and enterotoxigenic *E. coli* in young pigs (Genovese et al., 2003; Harvey et al., 2003). Researchers have also used CE in cattle as a strategy to eliminate *E. coli* O157:H7 as well as *Salmonella* (Zhao et al., 2003). Researchers used a defined population of multiple (non-O157:H7) *E. coli* strains that were isolated from cattle, and found this CE culture could displace an established *E. coli* O157:H7 population and could reduce the populations of *E. coli* O157:H7 in calves (Zhao et al., 1998). To date, this is the only true CE culture for cattle that is able to reduce foodborne pathogens and that is being developed as a commercial product.

Prebiotics

Sugars or other organic compounds not digested by the host animal but digestible by members of the microbial population are generally known as prebiotics (Walker and Duffy, 1998; Steer et al., 2000). Prebiotics can provide energy or other limiting nutrients to the intestinal mucosa and colonic or cecal bacterial fermentation, which can produce vitamins and antioxidants that benefit the host (Collins and Gibson, 1999; Crittenden, 1999). Additionally, some prebiotics can provide specific members of the native microflora (e.g., *Bifidobacteria*, *Lactobacillus*) that produce antimicrobial substances with a competitive advantage (Willard et al., 2000) that can directly inhibit pathogenic bacteria in a fashion similar to CE (Zopf and Roth, 1996). Coupling the use of CE and prebiotics, in a process known as synbiotics, could yield a synergistic effect in the reduction of foodborne pathogenic bacterial populations in food animals before slaughter. To date, however, the

use of prebiotics in food animals to reduce foodborne pathogens has been somewhat cost prohibitive.

Current Antipathogenic Strategies

Antipathogenic strategies are the most straightforward of the intervention strategies because they directly attack the pathogen of interest. However, because foodborne pathogenic bacteria typically do not have any unusual properties within the gut of food animals, they are difficult to target directly without significant "collateral damage" on the rest of the microbial population. However, a variety of antipathogen strategies can be used to address pathogen populations in food animals, including antibiotics and bacteriocins, bacteriophages, specific inhibition of pathogens, and vaccines.

Antibiotics and Bacteriocins or Colicins

The use of broad-spectrum antibiotics to control gastrointestinal pathogens, including foodborne pathogens, can so disrupt the intestinal microbial ecosystem that opportunistic pathogens are provided an opportunity to affect animal health, performance, or food safety deleteriously (Aarestrup and Wegener, 1999; Chopra and Roberts, 2001). Bacteria have many complex mechanisms to resist antibiotics, and the widespread use of antibiotics in both human medicine and animal agriculture has led to the widespread dissemination of antimicrobial resistance genes (Salyers and Shoemaker, 2006). Because of concerns about the dissemination of antimicrobial resistance, it is likely that prophylactic use of medically important antibiotics as growth promotants in food-producing animals will become completely prohibited.

Neomycin sulfate, an antibiotic approved for use in cattle, has a 24-h withdrawal period. Cattle that were fed neomycin for 48 h and that went through a 24-h withdrawal period shed significantly fewer generic *E. coli* and *E. coli* O157:H7 populations in their feces (Elder et al., 2002; Ransom et al., 2003). Ionophores are antimicrobials that improve cattle production efficiency by inhibiting gram-positive bacteria (Callaway et al., 2003), and it has been suggested that ionophores could provide gram-negative pathogens, such as *Salmonella* and *E. coli* O157:H7 pathogens, a competitive advantage. However, research has shown that ionophores do not alter pathogen populations in sheep or cattle, or in vitro (Edrington et al., 2003a,b, 2006; McAllister et al., 2006).

Some bacteria produce antimicrobial proteins that can inhibit the growth of foodborne pathogenic bacteria, including *E. coli*, *Salmonella*, and *Listeria* (Schamberger and Diez-Gonzalez, 2002; Stahl et al., 2004; Patton et al., 2007). These proteins are referred to as bacteriocins or colicins depending on their mode of action; however, these compounds open pores in susceptible bacterial membranes, causing these targets to "bleed" to death (Jack et al., 1995; Stroud et al., 1998). It has been shown that these antimicrobial proteins can inhibit *E. coli* strains pathogenic to swine in the gut (Stahl et al., 2004). These proteins can be protected to bypass ruminal or gastric degradation, and can be specifically released in the lower gut to target foodborne pathogens. Molecular techniques have allowed a scaling up of bacteriocins or colicin production to produce the proteins in sufficient quantities for use as feed additives to reduce foodborne pathogens in live animals (Hagens and Loessner, 2007).

Bacteriophages

Bacteria can be infected by bacterial viruses (or bacteriophages) that have very narrow target spectra, and some phages may be active against only a specific strain. This great degree of specificity allows phages to be used against targeted microorganisms in a mixed population without perturbing the microbial ecosystem, and phages have been used in place of antibiotics around the world. Bacteriophages are common natural members of the gastrointestinal microbial ecosystem of food animals (Adams et al., 1966; Orpin and Munn, 1973; Klieve and Bauchop, 1988). Bacteriophages have been used to control foodborne pathogenic bacteria in several species of food-producing animals, and have been used against specific animal pathogens (Smith and Huggins, 1987; Kudva et al., 1999; Huff et al., 2002). Several studies have examined the effect of phages on conditions or diseases that affect production efficiency or animal health (Smith and Huggins, 1982, 1983; Huff et al., 2002). To date, the effectiveness of phage treatment in the gut of animals has been variable (Raya et al., 2003, 2006). In 2007, a phage spray produced by Omnilytics (Salt Lake City, UT) specifically against *E. coli* O157:H7 on live cattle before slaughter was approved for use by the US Food and Drug Administration (**FDA**). Other researchers have developed phages as methods to reduce *Campylobacter* and *Salmonella* in live poultry and swine (Loc Carrillo et al., 2005; Toro et al., 2005; Wagenaar et al., 2005; Callaway et al., 2007) and by spraying them onto commercial meat products (Atterbury et al., 2003a; Goode et al., 2003). The use of phages as a pathogen reduction strategy has also been suggested as a spray on vegetables that are exposed to manure or farm runoff via irrigation.

Specific Inhibition of Pathogens via Metabolic Pathways

Salmonella and *E. coli* respire under anaerobic conditions by converting nitrate to nitrite via a dissimilatory nitrate reductase (Stewart, 1988). The intracellular bacterial enzyme nitrate reductase does not differentiate between nitrate and its analog chlorate, which is reduced to chlorite in the cytoplasm; chlorite accumulation kills bacteria (Stewart, 1988). Chlorate addition to swine diets reduced experimentally inoculated *Salmonella* and *E. coli* O157:H7 fecal and intestinal

populations (Anderson et al., 2001a,b). Other studies demonstrated that chlorate administered in drinking water significantly reduced *E. coli* O157:H7 populations in both cattle and sheep in the rumen, intestine, cecum, and feces (Callaway et al., 2002). Preliminary results examining the use of chlorate in broilers and in turkeys have yielded promising results as well (Byrd et al., 2003; Moore et al., 2006). Currently, chlorate has been licensed as a product and is under review by the US FDA.

Immunization to Prevent Pathogen Colonization

Methods to exploit the immune system of the animal to reduce foodborne pathogens have been studied. Traditionally, most veterinary vaccines for food animals were constructed to inhibit viruses and bacteria or their toxins that cause morbidity or mortality in animals; however, specific immunization has shown great promise in reducing concentrations of disease-causing pathogens in food animals. Vaccines against *Salmonella* strains responsible for disease have been developed for use in swine and dairy cattle (House et al., 2001). Vaccination has also been used successfully to combat postweaning *E. coli* edema disease in young pigs (Gyles, 1998) and to reduce *Salmonella* colonization in poultry (Zhang-Barber et al., 1999). More recently, vaccines that reduce fecal shedding of *E. coli* O157:H7 have been developed for use in cattle (Moxley et al., 2003; Judge et al., 2004). However, because *E. coli* O157:H7 and other enterohemorrhagic *E. coli* are shed sporadically by cattle, natural exposure to *E. coli* O157:H7 does not appears to confer protection to the host (Gyles, 1998). An anti-*E. coli* O157:H7 vaccine developed by Bioniche (Belleville, Ontario, Canada) was given conditional approval by the US FDA early in 2008.

Until recently, these anti-foodborne-pathogen vaccines have not been widely implemented in animal production systems because an economic incentive has been lacking. The introduction of "edible vaccines" has the potential to make immunization of food animals economically viable for many diseases, including foodborne pathogens. Thus, the use of vaccines specifically to eliminate or reduce targeted foodborne pathogens on the farm will likely increase in the future.

CURRENT RESEARCH ON FOOD SAFETY

Since the President's Food Safety Initiative was introduced in 1997, food safety research has remained fairly consistent (White House, Office of the Press Secretary, 1997). The Food Safety Initiative was formalized by a report titled, "Food Safety from Farm to Table: A National Food Safety Initiative—A Report to the President" (FDA, USDA, US Environmental Protection Agency, and Centers for Disease Control and Prevention, 1997). Relative to preharvest food safety, USDA remains the major agency contributing to food safety research. Each agency within USDA fills a necessary specific niche of research to help provide broad, overlapping coverage of the food safety area (Torrence, 2003) For example, the ERS conducts economic research and provides analyses of economic issues related to food safety and the food supply (http://www.ers.usda.gov/emphases/safefood; last accessed Feb. 26, 2008). The ERS has estimated the human illness costs of foodborne disease at $6.9 billion per year for the 5 major foodborne pathogens (Crutchfield and Roberts, 2000). The ERS also provides benefit-cost analyses of programs for food safety improvements. The ARS is the primary intramural research agency for USDA, with more than 2,200 scientists in 100 locations.

Current research includes the development of methodologies to detect and quantify pathogens, as well as the development of technologies for pathogen reduction both preharvest and postharvest. A close relationship with industry and other stakeholders provides the opportunity to transfer newly developed methodologies and technologies where needed in the field. Specific preharvest food safety research activities include the role of diet in the reduction of *E. coli* O157:H7, the development and use of probiotics for *Salmonella* reduction in poultry and swine, and understanding the risk factors and potential interventions for *Campylobacter* in poultry. Agricultural Research Service scientists, along with researchers at the University of California and funding from the Cooperative State Research Education and Extension Service (**CSREES**, USDA), provided expertise when the spinach outbreak occurred in 2006. An epidemiological study was conducted to evaluate the interactions of humans, animals, and the environment in the production of spinach and other leafy greens (Jay et al., 2007). The CSREES is the primary extramural research agency with a strong partnership with the land grant university system, which enables leadership in research, education, and extension programs. Through its competitive food safety grant programs [the National Research Initiative (**NRI**) and the National Integrated Food Safety Initiative] as well as other special grants, CSREES provides needed funding and direction for food safety research. The NRI is a major competitive granting program of CSREES. The Ensuring Food Safety Grant Program of the NRI funds more basic laboratory research, including molecular research or biotechnology. A strong emphasis has been on mechanisms, pathogenesis, and the use of new methods, such as biosensors, for the detection and reduction of foodborne pathogens. The Epidemiologic Approaches for Food Safety Grant Program within the NRI was established in 1999 and provides larger grants (up to $1.5 million) for epidemiological (population-type) studies. This is the only program funding these large epidemiological studies in food safety. The National Integrated Food Safety Initiative provides researchers an opportunity to link basic or applied research with an educational or extension program.

The Animal and Plant Health Inspection Agency (USDA) is primarily responsible for animal health issues and conducts National Animal Monitoring System Studies on different animal species each year. Although studies are focused on animal health issues, these national surveys provide useful preharvest food safety information, such as management practices and demographic data (http://www.aphis.usda.gov; last accessed Feb. 26, 2008). The Office of Public Health and Science within the Food Safety and Inspection Service (USDA) gathers and uses data in risk assessment development and implementation for decision and policy making. Several of these risk assessments have used preharvest data, but animal data continue to be incomplete. Within FDA, the Center for Veterinary Medicine has used food safety funding for research. Currently, the major component of funding is to continue and expand the National Antimicrobial Resistance Monitoring System. This system is a partnership among FDA, Centers for Disease Control and Prevention, and USDA to provide surveillance on the amounts of antimicrobial resistance among animals, humans, and now retail foods.

Future Directions of Food Safety Research

Despite all the research on preharvest food safety, there are still many unanswered questions. Preharvest food safety remains an important factor in the approach to food production and food safety from farm to table. Although an impact at the preharvest level will not solve all food safety issues, a reduction at one stage of production should logically produce an impact further down the production chain. Because of the complexity of the food production process, no one single prevention or intervention will eliminate foodborne risk. A major goal should be to determine a way to measure the impact of interventions at different phases of the production chain. Research is also needed to look at individual interventions and then interventions in combination. Economic analyses are also essential. Over the years, research has evolved from simply measuring the prevalence of foodborne organisms to identifying and evaluating risk factors, to understanding the transmission and persistence of foodborne organisms, to the development and implementation of interventions or mitigations and prevention or control strategies. This continues to be a major goal of research, with the ultimate goal of providing a reduction in foodborne illness.

As research questions have changed, so have the development and enhancement of methodological tools, yet this needs to continue, both in microbiology and in epidemiology. Although microbiological methods have improved, there is still a need for rapid, more sensitive and specific diagnostic tests for many of the foodborne pathogens. The ability to perform tests quickly and efficiently at the preharvest level would benefit researchers and producers. A major barrier for microbiologists at the pre- and postharvest levels is developing tests that can detect foodborne pathogens in complex matrices, such as in feces or in foods such as lettuce or cantaloupe. In parallel, epidemiologists need to provide more expertise in the development and implementation of sampling methods and designs so that new molecular techniques can be used for the best detection.

As data become more complex and more detailed, better analytical methods must be developed and used for interpretation. For example, enhanced molecular methods such as DNA fingerprinting, pulsed-field gel electrophoresis fingerprinting, and PCR have enabled researchers to determine intraspecific genomic diversity to study genotypes as well as phenotypes of foodborne pathogens, and to evaluate the clonal dissemination of genes. There is still confusion about how to interpret some of these data. Geographical information systems have also become a more popular tool. This technology has allowed epidemiologists to combine spatial and temporal data to follow the flow of organisms and to provide a better understanding of the role of the environment and ecology in foodborne disease. More advanced molecular tools will aid in the study of microbial ecology, genomics, and perhaps even cloned animals.

In summary, the goal of developing and implementing intervention and management strategies is the ideal, but to maintain visibility and gain resources for preharvest food safety research, measuring the impact and outcomes of these strategies is critical. The Institute of Medicine released a report in 2003 titled, "Scientific Criteria to Ensure Safe Food" (Committee on the Review of the Use of Scientific Criteria and Performance Standards for Safe Food, NRC, 2003). This report suggested developing microbiological standards and performance standards, food safety objectives, and public health objectives for food safety. Researchers in the postharvest area were quick to respond to these possibilities, particularly as regulatory agencies have provided standards, yet at the same time, this report also provides a needed framework for discussion at the preharvest level (Torrence, 2005). For example, can we determine a microbiological standard at the preharvest level? What is the most relevant measurement, and does it differ among microbial organisms? More important, how can we link a microbiological standard to a food safety objective or public health objective given that the food production chain contains many phases and multiple factors? Can we ultimately link preharvest interventions or prevention and control programs to a public health objective? This may be an unattainable goal, but it is important that some thought be given to even a simple measurement of outcome, not only for food safety, but also for ongoing research. The ability to measure and then present the success of research findings as well as the outcomes of interventions, preventions, and mitigations is important for universities and the government. Ultimately, these measurements can influence future funding, and even policy and decision making. The future of preharvest food safety research depends on the applicability to foodborne disease, foodborne illness, and public health.

Morality, Ethics, Food Safety, and the Future of Society and of the American Society of Animal Science

At the time the American Society of Animal Science was founded, the term food safety meant "Is this meat spoiled?" or "Will it kill consumers immediately?" Clearly, it was a market to which caveat emptor applied on a daily basis. The publication of *The Jungle* set in motion a flurry of events that are still active today. Food safety has evolved over the course of the century of existence of the American Society of Animal Science and the American Dairy Science Association, from being regarded as a luxury to being a fundamental human right. As a matter of course, the responsibility for food safety has shifted from being solely on the consumer to being on the government and the producer. This "three-legged stool" of shared responsibility has become more tilted in recent years, given that, with the litigious nature of society, someone is sought to blame for all foodborne illnesses. Thus, food producers are aware of the legal, ethical, and moral obligation to produce a safe product. Although the food supply in the United States is among the safest in the history of the world, which continues to grow safer, rare outbreaks of foodborne disease have become more widespread because of efficient distribution systems at the same time our tools for assigning direct responsibility for these tragic events have been sharpened.

Where do we go from here? That is largely up to us in the American Society of Animal Science and American Dairy Science Association as we develop new animal management systems to feed a growing world. As the number of people involved in agriculture continues to dwindle, the consumer disconnect with the reality of food supply chains will grow. Consequently, the core of our future mission as producers, researchers, and educators involved in food production is 1) to provide consumers with information about how to protect themselves (extending their leg of the "safety stool") and about how food is produced so they can make choices from a bewildering array of options in the marketplace today (organic vs. free range vs. the cheapest food available); and 2) to develop new methods to include consumers in our industry so that they understand the economic and moral issues faced by food producers in a globalized economy.

Conclusions

Knowledge derived through research in the last century has resulted in the development and use of new technologies that have markedly increased the efficiency of food production and created a huge animal production and food manufacturing industry capable of feeding the US population while also providing significant quantities of high-quality food for export to other countries. This has also created challenges to providing a safe and nutritious food supply. Given the considerable national and international demand and expectations for food safety and the formidable challenges of producing and maintaining a safe food supply, food safety research and educational programs have taken on a new urgency. Future scientific breakthroughs will no doubt have a profound impact on animal agriculture and on the production of high-quality food, but we will also be faced with moral, ethical, and societal dilemmas that must be reconciled. As the system of food production and distribution changes, the food safety system needs to change with it. A strong science-based approach that addresses all the complex issues involved in continuing to improve food safety and public health is necessary to prevent foodborne illnesses. Not only must research be conducted to solve complex food safety issues, but results of that research must also be communicated effectively to producers and consumers. Research and educational efforts identifying potential on-farm risk factors will better enable producers to reduce or prevent foodborne pathogen contamination of products leaving the farm. The identification of on-farm reservoirs and intervention strategies will aid in implementing farm-specific pathogen reduction programs. There is little doubt that solutions to these and many other complex issues will be delineated through science-based research that will be conducted during the next century. Members of the American Society of Animal Science and American Dairy Science Association will continue to be integral in finding and communicating solutions to complex food safety issues that will invariably result in a safe food supply for consumers.

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